UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,329	07/29/2003	Bryant G. Darnay	UTSC:761US	8033

32425 7590 02/28/2005

FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,329	DARNAY, BRYANT G.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2004 and 10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *10-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8 and 9* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/27/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence alignment.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-9, in the reply filed on 09/10/2004 and 12/21/2004 is acknowledged. Applicant's election of species without traverse of a Kaposifibroblast growth factor signal sequence is also acknowledged. Currently, claim 8 is generic regarding the leader signal sequences.
2. Claims 1-29 are pending. Claims 1-9 are under consideration. Claims 10-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse on 09/10/2004 and 12/21/2004

Information Disclosure Statement

3. The information disclosure statement submitted on 10/27/2003 has been considered by the Examiner and a signed copy has been attached to the office action.

Drawings

4. The drawings filed on 07/29/2003 are accepted by the Examiner.

Claim Rejections—35 USC § 112, 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for a genus of polypeptide comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 1-6, 8, and 9 are drawn to an isolated polypeptide comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure. Thus, the claims are broad and encompass virtually any random sequence of any length as long as the polypeptide comprises at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2. However, other than the polypeptide of SEQ ID NO: 2 and its encoding nucleic acids of SEQ ID NO: 1, the disclosure fails to provide sufficient guidance and/or working examples regarding the structural and functional requirements commensurate in scope with what is

encompassed by the instant claim. While disclosing three point mutations in RAIN that disrupt its inhibitory effect on ostoclast formation, the disclosure has not shown (i) which portions of SEQ ID NO: 2 are critical to the activity of the protein of SEQ ID NO: 2; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 2 will result in protein mutants with the same functions as the protein of SEQ ID NO: 2.

The relative skill of those in the art is not high because the prior art does not teach how to make and use the polypeptide of SEQ ID NO: 2, nor the genus of polypeptides comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2. It is noted that Tang et al. teach a polypeptide that is 98.9% identical to the polypeptide of SEQ ID NO: 2 of the present invention and comprises 163 contiguous amino acids of SEQ ID NO: 2 (U.S. Patnet Application Publication No. US 2003/0207430 A1, November 6, 2003; filing date March 1, 2001) and Demarini teach a polypeptide that is 98% identical to the polypeptide of SEQ ID NO: 2 of the present invention and comprises 93 contiguous amino acids of SEQ ID NO: 2 (Demarini (EP892050-A2, January 17, 1999). However, neither of the prior art establishes that the polypeptide has the same activity as that of RAIN of the present invention. It is unpredictable whether an isolated polypeptide comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2 shares the same activity with the polypeptide of SEQ ID NO: 2 due to lack of sufficient guidance provided in the specification and the teachings in the art on how to make and use the claimed genus of polypeptides. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser,

Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

Accordingly, while being enabling for an isolated polypeptide of SEQ ID NO: 2, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the genus of polypeptides comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections—35 USC § 112, 1st paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-6, 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of

complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-6, 8, and 9 are drawn to an isolated polypeptide comprising at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature. Thus, the claims encompass virtually any random sequence of any length as long as the polypeptide comprises at least 10, 15, 20, 30, or 50 contiguous amino acids of SEQ ID NO: 2.

The instant disclosure of an isolated polypeptide of SEQ ID NO: 2 and and its encoding nucleic acid molecule set forth in SEQ ID NO: 1 does not adequately support the scope of the claimed genus. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure discloses three point mutations in RAIN that disrupt its inhibitory effect on ostoclast formation, but fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no sufficient description of the conserved regions that are critical to the structure and function of the genus claimed. There is no sufficient description of the sites at which

variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polypeptides as being identical to those instantly claimed.

Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus. Accordingly, only the isolated polypeptide comprising SEQ ID NO: 2, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections—35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Demarini (EP892050-A2, January 17, 1999).

Demarini teach a polypeptide that is 98% identical to the polypeptide of SEQ ID NO: 2 of the present invention and comprises 93 contiguous amino acids of SEQ ID NO: 2 (see attached sequence alignment). Demarini further teach that it is oftern advantageous to include an additional amino acid sequence that contains secretory or leader sequences for stability during recombiant production (page 4, lines 52-53). Thus, the reference of Demarini meets the limitations of claims 1-6 and 8.

11. Claims 1-6 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (U. S. Patnet Application Publication No. US 2003/0207430 A1, November 6, 2003; filing date March 1, 2001).

Tang et al. teach a polypeptide that is 98.9% identical to the polypeptide of SEQ ID NO: 2 of the present invention and comprises 163 contiguous amino acids of SEQ ID NO: 2 (see attached sequence alignment). Tang et al. further teach that the polypeptide may have a leader sequence (a signal sequence). Thus, the reference of Tang et al. meets the limitations of claims 1-6 and 8.

Claim Objections

12. Claims 1-9 are objected to because of the following informalities: (i) there is an extra period at the end of claim 7; and (ii) claims 1-9 recite non-elected subject matter (non-elected amino acid sequences). Appropriate correction is required.

Conclusion

13. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
February 24, 2005

```
FT                   /note= "potential phosphorylation site"
FT   Modified-site   57
FT                   /note= "potential phosphorylation site"
FT   Modified-site   89
FT                   /note= "potential phosphorylation site"
FT   Modified-site   106
FT                   /note= "potential phosphorylation site"
FT   Modified-site   136
FT                   /note= "potential phosphorylation site"
FT   Modified-site   148
FT                   /note= "potential phosphorylation site"
FT   Modified-site   167
FT                   /note= "potential phosphorylation site"
FT   Modified-site   209
FT                   /note= "potential phosphorylation site"
FT   Modified-site   216
FT                   /note= "potential phosphorylation site"
FT   Modified-site   223
FT                   /note= "potential phosphorylation site"
XX
PN   WO200164896-A2.
XX
PD   07-SEP-2001.
XX
PF   01-MAR-2001; 2001WO-US006806.
XX
PR   01-MAR-2000; 2000US-0186307P.
PR   28-MAR-2000; 2000US-0192532P.
PR   30-MAR-2000; 2000US-0193578P.
XX
PA   (INCY-) INCYTE GENOMICS INC.
XX
PI   Tang YT, Lu DAM, Bandman O, Yue H, Azimzai Y, Lal P, Burford N;
PI   Baughn MR;
XX
DR   WPI; 2001-550184/61.
DR   N-PSDB; AAH75155.
XX
PT   Novel human enzyme molecule useful for treating and preventing, e.g.,
PT   cancer, genetic disorders, neurological disorders, autoimmune and
PT   inflammatory disorders.
XX
PS   Claim 1; Page 117; 154pp; English.
XX
CC   The present sequence represents a human enzyme. The enzyme polynucleotide
CC   and polypeptide are useful for diagnosis, treatment and prevention of
CC   cancers, neurological disorders (e.g. epilepsy, stroke, Alzheimer's
CC   disease, Pick's disease, Huntington's disease, dementia, multiple
CC   sclerosis, Parkinson's disease, amyotropic lateral sclerosis, bacterial
CC   and viral meningitis, schizophrenic disorders and neuroskeletal
CC   disorders), autoimmune/inflammatory disorders (e.g. allergies, addison's
CC   disease, autoimmune diseases, adult respiratory distress syndrome,
CC   anemia, asthma, Crohn's disease, atopic dermatitis, diabetes mellitus,
CC   osteoporosis, pancreatitis, psoriasis, rheumatoid arthritis, and viral,
CC   bacterial, fungal, parasitic, protozoal and helminthic infections),
CC   genetic disorder (e.g. Duchenne and Becker muscular dystrophy, Gaucher's
CC   disease, Huntington's chorea, sickle cell anemia, thalassemia, Von
CC   Willebrand's disease and Wilms' tumour), and cell proliferative disorder
CC   (e.g. atherosclerosis, leukemia, hepatitis, cirrhosis, and
CC   arteriosclerosis). The polynucleotide is also useful in somatic or
CC   germline gene therapy
XX
SQ   Sequence 242 AA;

  Query Match             98.9%;  Score 1307;  DB 4;  Length 242;
  Best Local Similarity   99.2%;  Pred. No. 1.4e-135;
  Matches  240;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGCDAREGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Db        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKDLKDRMAHA 180

Qy        181 MNEYRDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242


RESULT 4
AAW94762
ID   AAW94762 standard; protein; 242 AA.
XX
AC   AAW94762;
XX
DT   28-APR-1999  (first entry)
XX
DE   Amino acid sequence of human HFIZG53.
XX
KW   HFIZG53; human; inflammatory disease; infection; HIV-1; HIV-2; cancer;
KW   HIV-associated cachexia; immunodeficiency disorder; septic shock; pain;
KW   Parkinson's disease; cardiovascular disease; psychotic; neurological;
KW   Huntington's disease; Gilles de la Tourette's syndrome; gene mapping.
XX
OS   Homo sapiens.
XX
PN   EP892050-A2.
XX
PD   20-JAN-1999.
XX
PF   17-FEB-1998;   98EP-00301168.
XX
PR   08-JUL-1997;   97US-0051937P.
PR   17-OCT-1997;   97US-00953494.
XX
PA   (SMIK ) SMITHKLINE BEECHAM CORP.
XX
PI   Demarini DJ;
XX
DR   WPI; 1999-083567/08.
DR   N-PSDB; AAX05748.
XX
PT   New HFIZG53 polypeptide and polynucleotide - useful as diagnostic
PT   reagents and for prevention and treatment of inflammatory diseases,
PT   cancer and Parkinson's disease.
XX
PS   Claim 11; Page 7; 22pp; English.
XX
CC   This represents the amino acid sequence of human HFIZG53. Host cells
CC   containing an expression system comprising the HFIZG53 nucleic acid are
CC   used for the recombinant production of the protein. HFIZG53 polypeptides
CC   and polynucleotides are useful for diagnosing diseases related to over or
CC   underexpression of HFIZG53 protein. The HFIZG53 polypeptides can be used
CC   to screen for agonists and antagonists which can be used in treatment to
CC   activate or inhibit HFIZG53 activity. Gene therapy may also be used to
CC   affect endogenous polypeptide production, using HFIZG53 polynucleotides
CC   and retroviral vectors. HFIZG53 antibodies are useful for inducing an
CC   immune response to immunise and prevent diseases, and for isolating
CC   HFIZG53 clones or purifying the polypeptide by affinity chromatography.
CC   HFIZG53 polypeptides can be administered directly or as a vaccine to
CC   inoculate against disease. Diseases prevented, diagnosed or treated
CC   include inflammatory diseases such as Adult Respiratory Disease Syndrome,
CC   rheumatoid arthritis, osteoarthritis, inflammatory Bowel Disease, asthma,
CC   psoriasis, dermatitis, allergies; infections including bacterial, fungal,
CC   protozoan and viral, particularly HIV-1 and -2; HIV-associated cachexia
CC   and other immunodeficiency disorders; septic shock; injury; pain; cancers
```

CC including testicular cancer; anorexia; bulimia; Parkinson's disease;
CC cardiovascular disease including restenosis, atherosclerosis, acute heart
CC failure, myocardial infarction, hypotension, hypertension; urinary
CC retention; angina pectoris; ulcers; benign prostatic hypertrophy; and
CC psychotic and neurological disorders (anxiety, schizophrenia, delirium,
CC manic depression, dementia, severe mental retardation) and dyskinesias,
CC such as Huntington's diseases or Gilles de la Tourette's syndrome. The
CC HFIZG53 polypeptide is also useful for mapping the gene to a chromosome,
CC allowing gene inheritance to be studied through linkage analysis
XX
SQ Sequence 242 AA;

Query Match 98.0%; Score 1296; DB 2; Length 242;
Best Local Similarity 98.8%; Pred. No. 2.3e-134;
Matches 239; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

```
Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGCDAWEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGVQKERIQPEDMFVYDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKDLKDRMAHA 180

Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242
```

RESULT 5
AAY85636
ID AAY85636 standard; protein; 242 AA.
XX
AC AAY85636;
XX
DT 07-FEB-2001 (first entry)
XX
DE Antigen recognised by Ab capable of inducing G-CSF activity.
XX
KW Antigenic protein; antibody; granulocyte colony stimulating factor;
KW G-CSF; cancer therapy; bone marrow suppression; human.
XX
OS Homo sapiens.
XX
PN WO200060075-A1.
XX
PD 12-OCT-2000.
XX
PF 31-MAR-2000; 2000WO-JP002080.
XX
PR 01-APR-1999; 99JP-00099092.
XX
PA (NISB) JAPAN TOBACCO INC.
XX
PI Sha S, Aoki Y, Nishi Y;
XX
DR WPI; 2001-024452/03.
DR N-PSDB; AAC61150.
XX
PT Gene encoding an antigen recognizing an antibody which induces
PT granulocyte colony stimulating factor (G-CSF) expression for gene therapy
PT and treatment of G-CSF associated disorders e.g. the side effects of
PT cancer therapy.
XX
PS Claim 3; Page 52-53; 58pp; Japanese.

XX
CC The present invention relates to a gene encoding an antigenic protein
CC recognised by an antibody or its fragments which can induce the
CC production of granulocyte colony stimulating factor (G-CSF). Also
CC included in the invention are partial sequences of the gene, antibodies
CC recognising all or part of the antigenic protein, expression vectors
CC containing the gene and host cells transformed by the vector. The gene is
CC used for gene therapy, and compounds identified by screening using the
CC gene sequence are used for treatment and prevention of disorders
CC associated with G-CSF expression such as the side effects of cancer
CC therapy (including bone marrow suppression). The present sequence
CC represents the human antigen of the invention
XX
SQ Sequence 242 AA;

Query Match 98.0%; Score 1296; DB 4; Length 242;
Best Local Similarity 98.8%; Pred. No. 2.3e-134;
Matches 239; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

```
Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGCDAWEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGVQKERIQPEDMFVYDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKDLKDRMAHA 180

Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242
```

RESULT 6
AAU77178
ID AAU77178 standard; protein; 242 AA.
XX
AC AAU77178;
XX
DT 02-JUL-2002 (first entry)
XX
DE Human G-CSF-inducible antibody binding protein, MMR19.
XX
KW Human; granulocyte-colony stimulating factor; G-CSF; MMR19;
KW antimicrobial; G-CSF-inducible antibody; neutrophil deficiency disease;
KW infection.
XX
OS Homo sapiens.
XX
PN WO200226978-A1.
XX
PD 04-APR-2002.
XX
PF 27-SEP-2001; 2001WO-JP008446.
XX
PR 27-SEP-2000; 2000JP-00294191.
XX
PA (NISB) JAPAN TOBACCO INC.
XX
PI Sha S, Mukai H, Aoki Y, Nishi Y;
XX
DR WPI; 2002-340016/37.
DR N-PSDB; ABK47967.
XX
PT Gene encoding protein binding to antibody having granulocyte-colony
PT stimulating factor (G-CSF) inducing activity, useful for screening

```
Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242


RESULT 2
US-10-220-381-2
; Sequence 2, Application US/10220381
; Publication No. US20030207430A1
; GENERAL INFORMATION:
;  APPLICANT: INCYTE GENOMICS, INC.
;  APPLICANT:  TANG, Y. Tom
;  APPLICANT:  LU, Dyung Aina M.
;  APPLICANT:  BANDMAN, Olga
;  APPLICANT:  YUE, Henry
;  APPLICANT:  AZIMZAI, Yalda
;  APPLICANT:  LAL, Preeti
;  APPLICANT:  BURFORD, Neil
;  APPLICANT:  BAUGHN, Mariah R.
;  TITLE OF INVENTION: HUMAN ENZYME MOLECULES
;  FILE REFERENCE: PF-0763 PCT
;  CURRENT APPLICATION NUMBER: US/10/220,381
;  CURRENT FILING DATE:  2001-03-01
;  NUMBER OF SEQ ID NOS: 52
;  SOFTWARE: PERL Program
; SEQ ID NO 2
;   LENGTH: 242
;   TYPE: PRT
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: misc_feature
;   OTHER INFORMATION: Incyte ID No. US20030207430A1 2116390CD1
US-10-220-381-2

  Query Match             98.9%;  Score 1307;  DB 14;  Length 242;
  Best Local Similarity   99.2%;  Pred. No. 1.7e-127;
  Matches  240;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGCDAREGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKDLKDRMAHA 180

Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242


RESULT 3
US-10-381-710-4
; Sequence 4, Application US/10381710
; Publication No. US20040052789A1
; GENERAL INFORMATION:
;  APPLICANT: SHA, Shiken et al.
;  TITLE OF INVENTION: NOVEL PROTEINS, GENES ENCODING THEM AND METHOD OF USING THE SAME
;  FILE REFERENCE: 0230-0198P
;  CURRENT APPLICATION NUMBER: US/10/381,710
;  CURRENT FILING DATE:  2003-09-16
;  NUMBER OF SEQ ID NOS: 17
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 4
;   LENGTH: 242
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-381-710-4

  Query Match             98.0%;  Score 1296;  DB 15;  Length 242;
  Best Local Similarity   98.8%;  Pred. No. 2.3e-126;
  Matches  239;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGCDAWEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SGVQKERIQPEDMFVYDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKDLKDRMAHA 180

Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240

Qy        241 IV 242
              ||
Db        241 IV 242


RESULT 4
US-10-381-710-2
; Sequence 2, Application US/10381710
; Publication No. US20040052789A1
; GENERAL INFORMATION:
;  APPLICANT: SHA, Shiken et al.
;  TITLE OF INVENTION: NOVEL PROTEINS, GENES ENCODING THEM AND METHOD OF USING THE SAME
;  FILE REFERENCE: 0230-0198P
;  CURRENT APPLICATION NUMBER: US/10/381,710
;  CURRENT FILING DATE:  2003-09-16
;  NUMBER OF SEQ ID NOS: 17
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 2
;   LENGTH: 241
;   TYPE: PRT
;   ORGANISM: Mouse macrophage cell RAW 264.7
US-10-381-710-2

  Query Match             93.8%;  Score 1239.5;  DB 15;  Length 241;
  Best Local Similarity   93.8%;  Pred. No. 1.8e-120;
  Matches  227;  Conservative    9;  Mismatches    5;  Indels    1;  Gaps    1;

Qy          1 MSGCDAGEGDCCSRRCGAQDKEHPRYLIPELCKQFYHLGWVTGTGGGISLKHGDEIYIAP 60
              |||| | :|||||| |||||||||:|||||||||||||||||||||||:||||||
Db          1 MSGCQA-QGDCCSRPCGAQDKEHPRFLIPELCKQFYHLGWVTGTGGGISLKHGNEIYIAP 59

Qy         61 SGVQKERIQPEDMFVCDINEKDISGPSPSKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 120
              ||||||||||||||||||:|||||  |||||||||||||||||||||||||||||||||||
Db         60 SGVQKERIQPEDMFVCDINEQDISGPPASKKLKKSQCTPLFMNAYTMRGAGAVIHTHSKA 119

Qy        121 AVMATLLFPGREFKITHQEMIKGIKKCTSGGYYRYDDMLVVPIIENTPEEKGLKDRMAHA 180
              ||||||||||:|||||||||||:|||||||||||||||||||||||||| ||:||||||
Db        120 AVMATLLFPGQEFKITHQEMIKGIRKCTSGGYYRYDDMLVVPIIENTPEEKDLKERMAHA 179

Qy        181 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKVGLDPSQLPVGENG 240
              ||||||||||||||||||||||||||||||||||||||||||:||||:||||||||
Db        180 MNEYPDSCAVLVRRHGVYVWGETWEKAKTMCECYDYLFDIAVSMKKMGLDPTQLPVGENG 239

Qy        241 IV 242
```